

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (Currently Amended) An isolated antibody, or a derivative or a fragment thereof, having a binding structure for a target structure displayed in, and on the cell surface of, human gastrointestinal epithelial tumour cells and in a subpopulation of normal human gastrointestinal epithelial cells, said binding structure comprising the complementarity determining region (CDR) sequences in the light chain comprising essentially the amino acids number 23-33 (CDR1), 49-55 (CDR2), 88-98 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, and the CDR sequences in the heavy chain comprising essentially the amino acids number 158-162 (CDR1), 177-193 (CDR2), 226-238 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, or other binding structures with similar unique binding properties.

2. (Currently Amended) An isolated antibody according to claim 1, which is phage selected.

3. (Currently Amended) An isolated antibody according to claim 1, wherein the sequences are of *Macaca fascicularis* origin.

4. (Original) A derivative of an antibody according to claim 1, which is of human origin.

5. (Currently Amended) An isolated antibody according to claim 1, wherein the sequences have an identity of at least 84% to corresponding sequences of human origin.

6. (Currently Amended) An isolated antibody according to claim 1, which has low immunogenicity or non-immunogenicity in humans.

7. (Currently Amended) An isolated antibody according to claim 1, which has been derivatised by genetically linking to other polypeptides, and/or by chemical conjugation to organic or non-organic chemical molecules, and/or by di-, oligo- or multimerisation.

8. (Currently Amended) An isolated antibody according to claim 1, which is genetically linked or chemically conjugated to cytotoxic polypeptides or to cytotoxic organic or non-organic chemical molecules.

9. (Currently Amended) An isolated antibody according to claim 1, which is genetically linked or chemically conjugated to biologically active molecules.

10. (Currently Amended) An isolated antibody according to claim 1, which is genetically linked or chemically conjugated to immune activating molecules.

11. (Currently Amended) An isolated antibody according to claim 1, which has been changed to increase or decrease the avidity and/or affinity thereof.

12. (Currently Amended) An isolated antibody according to claim 1, which has been changed to increase the production yield thereof.

13. (Currently Amended) An isolated antibody according to claim 1, which has been changed to influence the pharmacokinetic properties thereof.

14. (Currently Amended) An isolated antibody according to claim 1, which has been changed to give new pharmacokinetic properties thereto.

15. (Currently Amended) An isolated antibody according to claim 1, which is labeled and the binding thereof is inhibited by an unlabeled form of said antibody and not by other binding structures, and not inhibiting the binding of other binding structures having other binding specificities.

16. (Currently Amended) An isolated antibody according to claim 1, wherein said binding structure recognizes a non-reduced form of $\alpha_6\beta_4$ integrin.

17. (Withdrawn) A target structure displayed in, or on the surface of, tumour cells, said target structure

- a) having the ability of being specifically blocked by and to specifically block the binding structure of an antibody as defined in claim 1, and other binding structures with similar binding properties,
- b) being displayed in, and on the surface of, human gastrointestinal epithelial cells,
- c) having substantial homology with $\alpha 6$ and/or $\beta 4$ integrin chains or variants thereof, representing a shared or unique epitope,
- d) being highly expressed on the surface of tumour cells, and
- e) being a target for cytotoxic effector mechanisms.

18. (Withdrawn) A target structure according to claim 17, wherein the binding structure is labeled and the binding thereof is inhibited by an unlabeled form of said binding structure and not by other binding structures, and not inhibiting the binding of other binding structures having other binding specificities.

19. (Withdrawn) A target structure according to claim 17, wherein said binding structure comprises one or more of the complementarity determining region (CDR) sequences comprising essentially the amino acids number 23-33, 49-55, 88-98, 158-162, 177-193, 226-238 of the amino acid sequence shown in SEQ ID NO:2, or other binding structures with similar unique binding properties.

20. (Withdrawn) A target sturcture according to claim 17, wherein said binding structure is an antibody.

21. (Withdrawn) A target structure according to claim 20, wherein said antibody comprises the variable region of a light chain comprising essentially the amino acids number 1-109 of the amino acid sequence shown in SEQ ID NO:2, and the variable region of a heavy chain comprising essentially the amino acids number 128-249 of the amino acid sequence shown in SEQ ID NO: 2.

22. (Withdrawn) A target structure according to claim 17, which is expressed homogenously in human colonic epithelial cells and less in pancreatic duct and bile duct cells.

23. (Withdrawn) A target structure according to claim 17, the expression of which is correlated to gastrointestinal epithelial differentiation.

24. (Withdrawn) A target structure according to claim 17, which comprises essentially the amino acid sequence of $\alpha 6$ integrin shown in SEQ ID NO: 3 and/or of $\beta 4$ integrin shown in SEQ ID NO: 4, and/or one or more fragments, and/or variants or splice variants, and or subunits, thereof.

25. (Withdrawn) A target structure according to claim 24, which comprises homo- or hetero-monomers or homo- or hetero-multimers of said $\alpha 6\beta 4$ integrin and/or of said one or more fragments and/or variants and/or subunits thereof.

26. (Withdrawn) A target structure according to claim 24, which has an apparent molecular weight in its non-reduced form of from 90 to 140 kDa, most preferred from 80 to 160 kDa.

27. (Withdrawn) A target structure according to claim 24, which comprises a peptide or polypeptide(s) comprising essentially any one of the amino acid sequences shown in SEQ ID NOs: 5-51, or comprises a molecule complexed to said polypeptide(s).

28. (Withdrawn) A target structure according to claim 24 recognised, exclusively or not, in its non-reduced form by the binding structure comprised by the antibody, or a derivative or a fragment thereof, having a binding structure for a target structure displayed in, and on the cell surface of, human gastrointestinal epithelial tumour cells and in a subpopulation of normal human gastrointestinal epithelial cells, said binding structure comprising the complementarity determining region (CDR) sequences in the light chain comprising essentially the amino acids number 23-33 (CDR1), 49-55 (CDR2), 88-98 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, and the CDR sequences in the heavy chain comprising essentially the amino acids number 158-162 (CDR1), 177-193 (CDR2), 226-238 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, or other binding structures with similar unique binding properties.

29. (Withdrawn) A substance which binds to the target structure as defined in claim 17, which substance is an organic chemical molecule or a peptide.

30. (Withdrawn) A substance, which is an anti-idiotype of a binding structure to said target structure as defined in claim 17.

31. (Withdrawn) A substance according to claim 30, which anti-idiotype is specifically blocked by and specifically blocks a binding structure having binding specificity for said target structure.

32. (Withdrawn) A substance which blocks the function of the target structure as defined in claim 17, which substance is an organic chemical molecule or a peptide.

33. (Withdrawn) A binding structure which recognizes a target structure as defined in claim 17, and which is of an organic chemical nature.

34. (Original) A pharmaceutical composition comprising as an active principle an antibody as defined in claim 1.

35. (Withdrawn) A pharmaceutical composition comprising as an active principle a target structure as defined in claim 17.

36. (Withdrawn) A pharmaceutical composition comprising as an active principle a substance as defined in claim 29.

37. (Currently Amended) A ~~vaccine~~ vaccine composition comprising as an active principle an antibody as defined in claim 1.

38. (Withdrawn) A method of therapy for treating conditions based on an anti-angiogenic mechanism, whereby an antibody as defined in claim 1 is administered to a human subject.

39. (Withdrawn) A method of treating human metastatic diseases, wherein an antibody as defined in claim 1 is administered to a human subject.

40. (Withdrawn) A method of in vitro histopathological diagnosis and prognosis of human malignant disease, whereby a sample is contacted with an antibody as defined in claim 1 and an indicator.

41. (Withdrawn) A method according to claim 40, which method comprises tumour typing.

42. (Withdrawn) A method according to claim 40, which method comprises tumour screening.

43. (Withdrawn) A method according to claim 40, which method comprises tumour diagnosis and prognosis.

44. (Withdrawn) A method according to claim 40, which method comprises monitoring premalignant conditions.

45. (Withdrawn) A method for in vitro diagnosis and prognosis of human malignant disease, whereby concentrations in bodily fluids of an antigen comprising a target structure as defined in claim 17.

46. (Withdrawn) A method for in vitro diagnosis and prognosis of human malignant disease, whereby concentrations in bodily fluids of an antibody as defined in claim 1 is assayed.

47. (Withdrawn) A method for in vitro diagnosis and prognosis of human malignant disease, whereby concentrations in bodily fluids of a complex of a) an antigen comprising a target structure, as defined in claim 17 is assayed, and b) an antibody, or a derivative or a fragment thereof, having a binding structure for a target structure displayed in, and on the cell surface of, human gastrointestinal epithelial tumour cells and in a subpopulation of normal human gastrointestinal epithelial cells, said binding structure comprising the complementarity determining region (CDR) sequences in the light chain comprising essentially the amino acids number 23-33 (CDR1), 49-55 (CDR2), 88-98 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, and the CDR sequences in the heavy chain comprising essentially the amino acids number 158-162 (CDR1), 177-193 (CDR2), 226-238 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, or other binding structures with similar unique binding properties, is assayed.

48. (Withdrawn) A method for in vivo diagnosis and prognosis of human malignant disease, whereby the localisation of an antibody, as defined in claim 1, to tumour deposits in a human subject is determined.

49. (Withdrawn) A method according to claim 48, whereby said antibody is administered to the subject before the determination.

50. (Withdrawn) A method according to claim 48, whereby said antibody is accumulated in tumour deposits.

51. (Withdrawn) A method according to claim 48 which is quantitative.

52. (Withdrawn) A method for therapy of human malignant disease, whereby an antibody, as defined in claim 1, is administered to a human subject.

53. (Withdrawn) A vaccine composition comprising as an active principle a target structure as defined in claim 17.

54. (Withdrawn) A vaccine composition comprising as an active principle a substance as defined in claim 29.

55. (Withdrawn) A method of therapy for treating conditions based on an anti-angiogenic mechanism, whereby a target structure as defined in claim 17 is administered to a human subject.

56. (Withdrawn) A method of therapy for treating conditions based on an anti-angiogenic mechanism, whereby a substance as defined in claim 29 is administered to a human subject.

57. (Withdrawn) A method for in vitro diagnosis and prognosis of human malignant disease, whereby concentrations in bodily fluids of a complex of a) a target structure, as defined in claim 29, is assayed, and b) an antibody or a derivative or a fragment thereof, having a binding structure for a target structure displayed in, and on the cell surface of, human gastrointestinal epithelial tumour cells and in a subpopulation of normal human gastrointestinal epithelial cells, said binding structure comprising the complementarity determining region (CDR) sequences in the light chain comprising essentially the amino acids number 23-33 (CDR1), 49-55 (CDR2), 88-98 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, and the CDR sequences in the heavy chain comprising essentially the amino acids number 158-162 (CDR1), 177-193 (CDR2), 226-238 (CDR3) of the amino acid sequence shown in SEQ ID NO:2, or other binding structures with similar unique binding properties, is assayed.